

What is claimed is:

1. A method of efficiently culturing a chimeric adenovirus in a selected host cell, said chimeric adenovirus being from a parental adenovirus strain incapable of efficient growth in said host cell, said method comprising the steps of:

(a) generating a chimeric adenovirus comprising:

(i) adenovirus sequences of the left terminal end and right terminal end of a first adenovirus which grows in a selected host cell type, said left end region comprising the 5' inverted terminal repeat (ITRs), and said right end region comprising the 3' inverted terminal repeat (ITRs); and

(ii) the internal regions from a parental adenovirus which lacks its native 5' and 3' terminal regions, said internal regions comprising the late genes encoding the penton, hexon, and fiber;

wherein the resulting chimeric adenovirus comprises, from 5' to 3', a left terminal region of the first adenovirus, the internal region of the parental adenovirus, and the right terminal region of the first adenovirus; and

b) culturing said chimeric adenovirus in the presence of functional adenovirus E1a, E1b, and E4 ORF6 genes from the first adenovirus or from an adenovirus serotype which transcomplements the first adenovirus, and further in the presence of necessary adenoviral structural genes from the left end of the adenovirus.

2. The method according to claim 1, wherein the internal region of the parental adenovirus further comprises one or more functional adenovirus genes selected from the group consisting of Endoprotease open reading frame, DNA binding protein, 100 kDa scaffolding protein, 33 kDa protein, protein VIII, pTP, 52/55 kDa protein, protein VII, Mu and protein VI.

3. The method according to claim 1, wherein the polymerase, terminal protein and 52/55 kDa protein functions are provided in *trans*.

4. The method according to claim 1, wherein the first adenovirus further comprises the polymerase, terminal protein and 52/55 kDa protein functions.
5. The method according to claim 1, wherein the chimeric adenovirus comprises the adenoviral late genes 1, 2, 3, 4, and 5 of the parental adenovirus.
6. The method according to claim 1, wherein the selected host cell stably contains one or more of the adenovirus E1a, E1b or E4 ORF6 functions.
7. The method according to claim 1, wherein the chimeric adenovirus comprises one or more of the adenovirus E1a, E1b or E4 ORF6 of the first adenovirus.
8. The method according to claim 1, wherein the first adenovirus is of human origin.
9. The method according to claim 1, wherein the first adenovirus is of simian origin.
10. The method according to claim 1, further comprising the step of isolating the chimeric adenovirus.
11. A method for generating a chimeric adenovirus for growth in a selected host cell, said chimeric adenovirus being derived from a parental adenovirus strain incapable of efficient growth in said host cell, said method comprising the step of generating a chimeric adenovirus comprising:
  - 5' and 3' terminal regions of a first adenovirus which grows in a selected host cell type, said 5' terminal regions comprising the 5' inverted terminal repeat (ITRs) and necessary E1 gene functions, and said 3' terminal regions comprising inverted terminal repeat (ITRs) and necessary E4 gene functions; and
  - internal regions from a parental adenovirus which lacks its native 5' and 3' terminal regions, said internal regions comprising the hexon, penton base and fiber;

wherein the resulting chimeric adenovirus comprises, from 5' to 3', the 5' terminal region of the first adenovirus, the internal region of the parental adenovirus, and the 3' terminal regions of the first adenovirus.

12. A chimeric adenovirus produced according to the method of claim 1.

13. A chimeric adenovirus comprising a hexon protein of a selected adenovirus serotype which is incapable of efficient growth in a selected host cell, said modified adenovirus comprising:

(a) adenovirus sequences of the left terminal end of a first adenovirus which grows in a selected host cell type, said left end region comprising the E1a, E1b and 5' inverted terminal repeat (ITRs);

(b) adenovirus sequences of the internal region of the selected adenovirus serotype which is incapable of efficient growth in the selected host cell, said internal region comprising the genes encoding the penton, hexon and fiber of the selected adenovirus;

(c) adenovirus sequences of the right terminal end of the first adenovirus, said right end region comprising the necessary E4 gene functions and the 3' inverted terminal repeat (ITRs),

wherein the resulting chimeric adenovirus comprises adenoviral structural and regulatory proteins necessary for infection and replication.

14. The chimeric adenovirus according to claim 13, wherein the chimeric adenovirus further comprises the IIIa, 52/55kDa and terminal protein (pTP) of the selected adenovirus serotype.

15. The chimeric adenovirus according to claim 13, wherein chimeric adenovirus comprises the polymerase of the first adenovirus.

16. The chimeric adenovirus according to claim 13, wherein the chimeric adenovirus expresses a functional chimeric protein formed from the first adenovirus and the selected adenovirus, said chimeric protein is selected from the group consisting of polymerase, terminal protein, 52/55 kDa protein, and IIIa.

17. The chimeric adenovirus according to claim 13, wherein the chimeric adenovirus comprises the terminal protein, 52/55 kDa, and/or IIIa of the selected adenovirus.

18. A host cell comprising a chimeric adenovirus according to claim 12.

19. The host cell according to claim 18, wherein said host cell is a human cell.

20. An isolated simian adenovirus nucleic acid sequence selected from the group consisting of:

(a) SA18 having the sequence of nucleic acids 1 to 31967 of SEQ ID NO:12 and

(b) a nucleic acid sequence complementary to the sequence of any of (a) to (f).

21. An isolated simian adenovirus serotype nucleic acid sequence selected from one or more of the group consisting of:

(a) 5' inverted terminal repeat (ITR) sequences;

(b) the adenovirus E1a region, or a fragment thereof selected from among the 13S, 12S and 9S regions;

(c) the adenovirus E1b region, or a fragment thereof selected from among the group consisting of the small T, large T, IX, and IVa2 regions;

(d) the E2b region;

(e) the L1 region, or a fragment thereof selected from among the group consisting of the 28.1 kD protein, polymerase, agnoprotein, 52/55 kD protein, and IIIa protein;

(f) the L2 region, or a fragment thereof selected from the group consisting of the penton, VII, VI, and Mu proteins;

(g) the L3 region, or a fragment thereof selected from the group consisting of the VI, hexon, or endoprotease;

(h) the 2a protein;

- (i) the L4 region, or a fragment thereof selected from the group consisting of the 100 kD protein, the 33 kD homolog, and VIII;
- (j) the E3 region, or a fragment thereof selected from the group consisting of E3 ORF1, E3 ORF2, E3 ORF3, E3 ORF4, E3 ORF5, E3 ORF6, E3 ORF7, E3 ORF8, and E3 ORF9;
- (k) the L5 region, or a fragment thereof selected from a fiber protein;
- (l) the E4 region, or a fragment thereof selected from the group consisting of E4 ORF7, E4 ORF6, E4 ORF4, E4 ORF3, E4 ORF2, and E4 ORF1; and
- (m) the 3' ITR, of any of SA18 SEQ ID NO:12, or a sequence complementary to any of (a) to (m).

22. A simian adenovirus protein encoded by the nucleic acid sequence according to claim 21.

23. A composition comprising a simian adenovirus capsid protein according to claim 22 linked to a heterologous molecule for delivery to a selected host cell.

24. A method for targeting a cell having an adenoviral receptor comprising delivering to a subject a composition according to claim 23.

25. A nucleic acid molecule comprising a heterologous simian adenoviral sequence according to claim 21.

26. The nucleic acid molecule according to claim 25, wherein said simian adenoviral sequence encodes an adenoviral gene product and is operatively linked to regulatory control sequences which direct expression of the adenoviral gene product in a host cells.

27. The nucleic acid molecule according to claim 25, wherein said simian adenoviral sequence comprises the E1a region of SA18 SEQ ID NO:12.

28. A pharmaceutical composition comprising the nucleic acid molecule according to claim 27 and a physiologically compatible carrier.
29. A recombinant adenovirus having a capsid comprising a protein selected from the group consisting of:
- (a) a hexon protein of SA18, SEQ ID NO 13, or a unique fragment thereof;
  - (b) a penton protein of SA18, SEQ ID NO: 14, or a unique fragment thereof;
  - (c) a fiber protein of SA18, SEQ ID NO: 15, or a unique fragment thereof.
30. The recombinant adenovirus according to claim 29, wherein the capsid is of an artificial serotype.
31. The recombinant adenovirus according to claim 29, wherein said virus further comprises a heterologous gene operatively linked to sequences which direct expression of said gene in a host cell.
32. The recombinant adenovirus according to claim 29, further comprising 5' and 3' adenovirus cis-elements necessary for replication and encapsidation.
33. The recombinant adenovirus according to claim 29, wherein said vector lacks all or a part of the E1 gene.
34. A host cell comprising a heterologous nucleic acid molecule comprising the nucleic acid sequence according to claim 21.
35. The host cell according to claim 34, wherein said host cell is stably transformed with the nucleic acid molecule.

36. The host cell according to claim 34, wherein said host cell expresses one or more adenoviral gene products from said nucleic acid molecule, said adenoviral gene products selected from the group consisting of E1a, E1b, E2a, and E4 ORF6.

37. The host cell according to claim 34, wherein said host cell is stably transformed with a nucleic acid molecule comprising the simian adenovirus inverted terminal repeats.

38. A composition comprising a recombinant virus according to claim 29 in a pharmaceutically acceptable carrier.

39. A method for delivering a heterologous gene to a mammalian cell comprising introducing into said cell an effective amount of the recombinant virus according to claim 29.

40. A method for repeat administration of a heterologous gene to a mammal comprising the steps of:

- (a) introducing into said mammal a first vector which comprises the heterologous gene and
- (b) introducing into said mammal a second vector which comprises the heterologous gene;  
wherein at least the first virus or the second vector is a virus according to claim 29 and wherein the first and second recombinant vector are different.

41. A method for producing a selected gene product comprising infecting a mammalian cell with the recombinant virus according to claim 29, culturing said cell under suitable conditions and recovering from said cell culture the expressed gene product.

42. A method for eliciting an immune response in a mammalian host against an infective agent comprising administering to said host an effective amount of the

recombinant adenovirus of claim 29, wherein said heterologous gene encodes an antigen of the infective agent.

43. The method according to claim 42, comprising the step of priming the host with a DNA vaccine comprising the heterologous gene, prior to administering the recombinant adenovirus.